

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

Appl. No.: 09/977,260

#6

CTCGCTCCAAGTTGTGCAGCCGGACCGCCTCGGGGTGTGCAGCCGGCTCGCGAGGCCCTCCTGGGGCGGGCGGGGGCGCTCGGG 90

GGCCCCCTGAGCAGAAACAGGAAGAACAGGCTCGGTCCAGTGGCACCAGCTCCCTACCTCCTGTGCCAGCCCGCTGGCCTGTGGCA 180

GGCCATTCCCAGCGTCCCGACTGTGACCACTTGCTCAGTGTGCTCTCACCTGCCTCAGTTTCCCTCTGGGGGGGATGGCGGGCGAG 270

M A G R

SmaI

GCTCTCTGGTTTCTGGCGGGCATTTCACGGCTGTGATTCTGCTGAGGAACCTCCCGGGTGAGCCCCGGTTCTCCGAGCCTGGCACC 360

G S L V S W R A F H G C D S A E E L P R V S P R F L R A W H

SmaI

CCCCCTCCCGTCTCAGCCAGGATGCCAAGAGGGCGCTGGGCCCCGGGCACCCAGTGTATCACCAAATGCGAGCACACCCGCCCAAGCCAG 450

P P P V S A R M P T R R W A P G T Q C I T K C E H T R P K P

SmaI KpnI

GGGAGCTGGCCTTCGCAAGGGCGACGTGGTCACCATCCTGGAGCCTGGGAGAACAAGAGCTGGTACCGGTCAAGCACCACCCAGTG 540 SH 3

G E L A F R K G D V V T I L E A C E N K S W Y R V K H H T S

PvuII

GACAGGAGGGCTGCTGGCAGCTGGCGCGCTGGCGAGCGGAGGCCCTCTCCGAGACCCCAAGCTCAGCCTCATGCCGTGGTTCCAGG 630

G Q E G L L A A G A L R E R E A L S A D P K L S L M P W F H

PvuII PstI

GGAAGATCTCGGGCCAGGAGGCTGTCCAGCAGCTGCAGCCTCCGAGGATGGGCTGTTCTCGGTGCGGAGTCCGCGGCCACCCCGGGG 720

G K I S G Q E A V Q Q L Q P P E D G L F L V R E S A R H P G SH 2

ClaI

ACTACGTCTGTGCGTGAGCTTTGGCCGGCAGTCCACTACCGCGTCTGCACCGCGACGGCCACCTCACAATCGATGAGCCGTGT 810

D Y V L C V S F G R D V I H Y R V L H R D G H L T I D E A V

TCTTCTGCAACCTCATGGACATGCTGCAGCATTACAGCAAGACAAGCGCGCTATCTGCACCAAGCTGCTGAGACCAAAGCGGAAACAG 900

F F C N L M D M V E H Y S K D K G A I C T K L V R P K R K H

FIG.1A

e: NOVEL MEGAKARYOCYTIC PROTEIN

## TYROSINE KINASES

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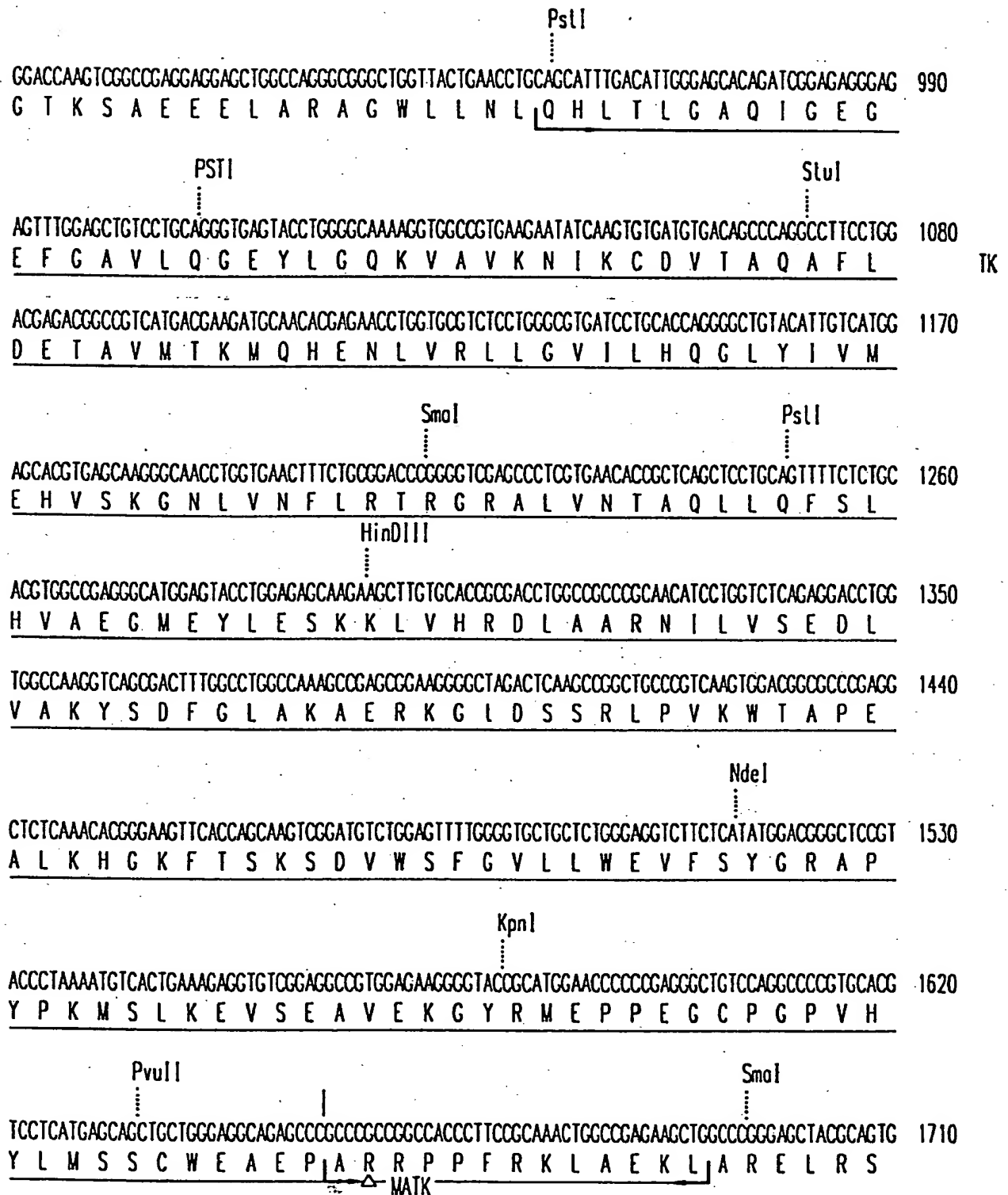


FIG.1B

## NOVEL MEGAKARYOCYTIC PROTEIN

## TYROSINE KINASES

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CAGGTGCCCCAGCCTCCGTCTCAGGGCAGGACGCGACGGCTCCACCTCGCCCCGAAGCCAGGAGCCCTGACCCCA<sup>1</sup>CCCGTGGGGCCCT 1800  
A G A P A S V S G Q D A D G S T S P R S Q E P

TGGCCCCAGAGACCCAGAGAGTGGAGAGTGGGGCTGGGGGCACTGACCAGGCCCAAGGAGGTCCAGGCGGGCAAGTCATCCTCCTGG 1890

TGCCACAGCAGGGGCTGCCCCACGTACGGGGCTCTGGCGGCCCCGTGGACACCCAGACCTGCCAAGGATGATCGCCCGATAAAGACCG 1980

ATTCTAAGGACTCTAAAAA 2000

FIG.1C

NOVEL MEGAKARYOCYTIC PRO  
TYROSINE KINASES

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CCGCTTTTGCITAGAGCTTGAGAGTCAAG AGGACCCACATGTATACITCGGCTCTAGCGAGT AGGATGATAATATGGATACA 90  
M D T

AAATCTATTCTAGAAGAACTTCTTCTCAAAAGATCACAGCAAAAGAAGAAATGTCACCAATAATTACAAGAACCGCTTTTGTITTC 180  
K S I L E E L L L K R S Q Q K K K M S P N N Y K E R L F V L

ACCAAAACAAACCTTTCTACTATGAATATGACAAAATGAAAACGGGCAGCAGAAAAGGATCCATTGAAATTAAGAAAATCAGATGTGTG 270  
T K T N L S Y Y E Y D K M K R G S R K G S I E I K K I R C V

GAGAAAGTAAATCTCGAGGAGCAGACGCCCTGTAGAGAGACAGTACCCATTTGAGATTGCTCTATAAAGATGGGCTTCTCTATGTCTATGCA 360  
E K V N L E E Q T P V E R Q Y P F Q I V Y K D G L L Y V Y A PH

TCAAATGAAGAGAGCCGAAGTCAGTGGTTCAAAGCATTACAAAAGAGATAACGGGTAACCCCCACCTGCTGGTCAAGTACCATAGTGGG 450  
S N E E S R S Q W L K A L Q K E I R G N P H L L V K Y H S G

TTCTTCGTGGACCGGAAGTTCTGTGTTGCCAGCAGAGCTGTAAGCAGCCCCAGGATGTACCCTCTGGAAGCATATGCTAATCTGCAT 540  
F F V D G K F L C C Q Q S C K A A P G C T L W E A Y A N L H

ACTGCAGTCAATGAAGAGAAACACAGAGTCCACCTTCCACAGACAGAGTGGTGAAGATACCTCGGGCAGTTCTGTCTCAAAATGGAT 630  
T A V N E E K H R V P T F P D R V L K I P R A V P V L K M D

GCACCATCTTCAAGTACCACTCTAGCCCAATATGACAACGAATCAAAGAAAACCTATGGCTCCAGCCACCATCTTCAAGTACCACTCTA 720  
A P S S S T T L A Q Y D N E S K K N Y G S Q P P S S S T S L SH3

GCGCAATATGACAGCAACTCAAAGAAAATCTATCGCTCCAGCCAACTTCAACATGCAGTATATTCCAAGGGAAGACTTCCCTGACTGG 810  
A Q Y D S N S K K I Y G S Q P N F N M Q Y I P R E D F P D W

TGCAAGTAAGAAAACCTGAAAAGTAGCAGCAGCAGTGAAGATGTTGCAAGCAGTAACCAAAAAGAAAGAAATGTAATCACACCACCTCA 900  
W Q V R K L K S S S S S S E D V A S S N Q K E R N V N H T T S

AAGATTTGATGGGAATTCCTCAGTCAAGTTCATCTGAAGAAGAGGAAAACCTCGATGATTATGACTGGTTTGTCTGTAACATCTCCAGA 990  
K I S W E F P E S S S S S E E E E N L D D Y D W F A G N I S R

TCACAATCTGAACAGTTACTCAGACAAAAGGAAAAGAGGAGCATTATGTTAGAAATTCAGCCAAAGTGGGAATGTACACAGTGTCC 1080  
S Q S E Q L L R Q K G K E G A F M V R N S S Q V G M Y T V S SH4

TTATTTAGTAAGCTGTGAATGATAAAAAAGCAACTGTCAAACATTACCAGTGCATACAAATGCTGAGAACAAATTATACCTGGCAGAA 1170  
L F S K A V N D K K G V K H Y H V H T N A E N K L Y L A E

FIG.2A

Title: NOVEL MEGAKARYOCYTIC PROTEIN

TYROSINE KINASES

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AACTACTGTTTTCATTCCATTCCAAAGCTTATTCATTATCATCAACACAATTACAGCAGCATGATCACACGGCTCCGCCACCCTGTGTCA 1260  
 N Y C F D S I P K L I H Y H Q H N S A G M I T R L R H P V S

ACAAAGCCCAACAAGCTCCCGACTCTGTGTCCCTCGGAAATGGAATCTGGAACTGAAAAGAGAAGATTACCTTGTGAAGGAGCTG 1350  
 T K A N K V P D S V S L G N G I W E L K R E E I T L L K E L

GGAAGTGGCCAGTTTGGAGTGGTCCAGCTCGGCAAGTGAAGGGGAGTATGATGTTGCTGTTAAGATGATCAAGGAGGGCTCCATGTCA 1440  
 G S G Q F G V V Q L G K W K G Q Y D V A V K M I K E G S M S

GAAGTGAATTTTCAGGAGGCCAGACTATGATGAACTCAGCCATCCCAAGCTCGTTAAATTCTATGAGTGTGTTCAAAGGAATAC 1530  
 E D E F F Q E A Q T M M K L S H P K L V K F Y G V C S K E Y

CCCATATACATAGTACTGAATATATAAGCAATGGCTGCTTCTGTAATTACCTGAGGAGTCACGGAAAAGGACTTGAACCTTCCCAGCTC 1620 TK  
 P I Y I V T E Y I S N G C L L N Y L R S H G K G L E P S Q L

TTAGAAATGTCTACGATGTCTGTGAAGCATGGCCTTCTTGGAGAGTCACCAATTCATACACGGGACTTGGCTGCTCGTAAGTCTTG 1710  
 L E M C Y D V C E G M A F L E S H Q F I H R D L A A R N C L

GTGGACAGAGATCTCTGTGTGAAAGTATCTGACTTTGGAATGACAAGGTATGTTCTTGATGACCAGTATGTCAGTTCAGTCCGAACAAAG 1800  
 V D R D L C V K V S D F G M T R Y V L D D Q Y V S S V G T K

TTTCCAGTCAAGTGGTCAGCTCCAGAGGTGTTTCATTACTTCAAATACAGCAGCAAGTCAGACGTATGGGCATTGGGATCCTGATGTGG 1890  
 F P V K W S A P E V F H Y F K Y S S K S D V W A F G I L M W

GAGGTGTTACGCTCGGGAAGCAGCCCTATGACTTGTATGACAACTCCAGGTGGTTCTGAAGGTCTCCAGGGCCACAGGCTTTACCGG 1980  
 E V F S L G K Q P Y D L Y D N S Q V V L K V S Q G H R L Y R

CCCCACCTGGCATCGGACACCATCTACCAGATCATGTACAGCTGCTGGCAGAGCTTCCAGAAAAGCGTCCACATTTACGAACTCCTG 2070  
 P H L A S D T I Y Q I M Y S C W H E L P E K R P T F Q Q L L

TCTTCCATTGAACCACTTCGGGAAAAAGACAAGCATTGAAGAAGAAATTAGGAGTGTGATAAGAATGAATATAGATGCTGGCCAGCATT 2160  
 S S I E P L R E K D K H

TTCATTCAATTTAAGGAAAGTAGCAAGGCATAATGTAATTTAGCTAGTTTTAATAGTGTCTCTGTATTGCTATTATTTAGAAATGAA 2250

CAAGGCAGGAAACAAAGATTCCCTTGAAATTTAGGTCAAATTAGTAATTTTGTATTGCTGCCCCGTATATAACACTTTCCAGCCTATA 2340

GCAGAAGCACATTTTCAGACTGCAATATAGAGACTGTGTTTCATGTGTAAGACTGAGCAGAACTGAAAAATTACTTATTGGATATTTCATT 2430

CTTTTCTTTATATTGTCATTGTCACAACAATTAATATACTACCAAGTACAAAAAAAAAAAAAAAAAAAAA 2500

FIG.2B

Title: NOVEL MEGAKARYOCYTIC PROTEIN

TYROSINE KINASES

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CCGGACTGGTCCGAAAGACAGGAACAGACTTGAACAGGGGAGAGCTCTGGCGAAACGAAGACGTGGAGGTTTTACCAGGATAAGAAG 90  
 AAAAGACACCTTCTAGTGAGCAGCTGCCAGCTCTGCTCAGTTTTGCCTCGGGTAGCACCTCCAGCCACAGAAAGCAAGCCGGTAAG 180  
 TCTCTCCAGGTAGGACTTGTGCAACCCAGCTGCTGGACTGATCTGAAACGGGACITTCATACTCTCCGAAGTATGGTGAGTTGGTGCT 270  
 M V S W C  
 GACTTCAAAGTTGCCTGGTGAAGGAAGATAAGGTGGATCCGAGAGCTAAGGGAGAGGAGAAGCCCTGCTCTTCTCCCCACCAAG 360  
 GCACAATGAGCAACATCTGTGACAGCCTCTGGAGTACCTAGAACCCTATCTCCCTGTTTGTCCACGGAGGCAGACAAGTCAACCGTGA 450  
 M S N I C Q R L W E Y L E P Y L P C L S T E A D K S T V  
 TTGAAATCCAGGGCGCTTTGCTCTCCCAGTCACAGAGGCATGGCCACTACTTTTGGCTTTGTTTGATTACCAGGCTCGGACTGCTG 540  
 I E N P G A L C S P Q S Q R H G H Y F V A L F D Y Q A R T A  
 AGGACTTGAGCTTCCGAGCAGGTGACAACTTCAAGTCTCGACACTTTGCATGAGGGCTGGTGGTTTCCAGACACTTGGAGAAAAGAC 630 SH 3  
 E D L S F R A G D K L Q V L D T L H E G W W F A R H L E K R  
 GAGATGGCTCCAGTCAGCAACTACAAGCCTATATTCCTTCTAACTACGTGGCTGAGGACAGAAGCCTACAGGCAGACCGTGGTTCTTTG 720  
 R D G S S Q Q L Q G Y I P S N Y V A E D R S L Q A E P W F F  
 GAGCAATCGGAAGATCAGATGCAGAGAAACAATATTATATTCAGAAAACAAGACCGGTTCTTTCTAATCAGAGAAAGTGAAAGCCAAA 810  
 G A I G R S D A E K Q L L Y S E N K T G S F L I R E S E S Q SH 2  
 AAGGAGAATTCTCTTTTCAGTTTTAGATGGAGCAGTTGTAAACACTACAGAATTAAGACTGGATGAAGCGGATTTTTTCTCACGC 900  
 K G E F S L S V L D G A V V K H Y R I K R L D E G G F F L T  
 GAAGAAGAATCTTTTCAACACTGAACGAATTTGTGAGCCACTACACCAAGACAAGTGACCGCCTGTGTGTCAAGCTGGGAAACCATGCT 990  
 R R R I F S T L N E F V S H Y T K T S D G L C V K L G K P C  
 TAAAGATCCAGGTCCAGCTCCATTGATTTGCTGATAAAACCGTGGACCAATCGGAGATAGACCGCACTCCATACAGCTTCTGAAGC 1080  
 L K I Q V P A P F D L S Y K T V D Q W E I D R N S I Q L L K  
 GATTGGATCTGGTCAGTTTGGCGAAGTATGCGAAGTCTGTGGAACAATACCACTCCAGTAGCAGTGAACATTAAACCAGGTTCAA 1170  
 R L G S G Q F G E V W E G L W N N T T P V A V K T L K P G S  
 TGGATCCAATGACTTCCTGAGGAGGCACAGATAATGAAGAACCTAAGACATCCAAGCTTATCCAGCTTTATGCTGTTTGCACCTTAG 1260  
 M D P N D F L R E A Q I M K N L R H P K L I Q L Y A V C T L

FIG.3A

TYROSINE KINASES

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|            |        | <u>MKK1</u> | <u>MKK2</u> |
|------------|--------|-------------|-------------|
| HUMAN      |        |             |             |
| MEG/ERYTH  | MEG-01 | +++         | +++         |
|            | K562   | ++          | +           |
|            | MO7E   | ++          | +           |
|            | HEL    | +++         | ++          |
| MYELO/MAC  | KG-1   | +           | ++          |
|            | HL-60  | +           | +           |
|            | TF-1   | +           | +           |
| B-CELL     | ALL-1  | -           | +           |
|            | RAJI   | -           | -           |
|            | DAUDI  | -           | -           |
| T-CELL     | MOLT-3 | -           | -           |
|            | JURKAT | -           | -           |
| EPITHELIAL | HELA   | -           | -           |
| RODENT     |        |             |             |
|            | BM     | +           | +++         |
|            | SPLEEN | +++         | +           |
|            | THYMUS | -           | -           |
|            | LIVER  | -           | -           |
|            | BRAIN  | +           | -           |
| RAT NEURAL | P19    | +           | -           |

FIG.4

Title: NOVEL MEGAKARYOCYTIC PROTEIN

09977260.050802

TYROSINE KINASES

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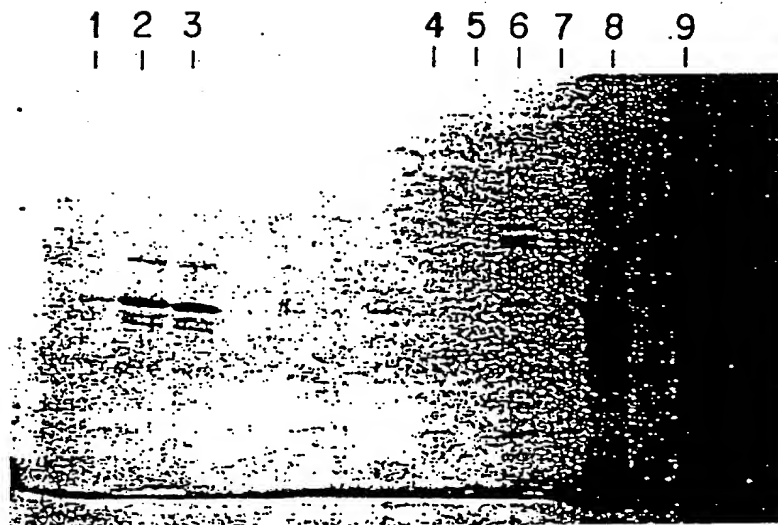


FIG. 5

BEST AVAILABLE COPY



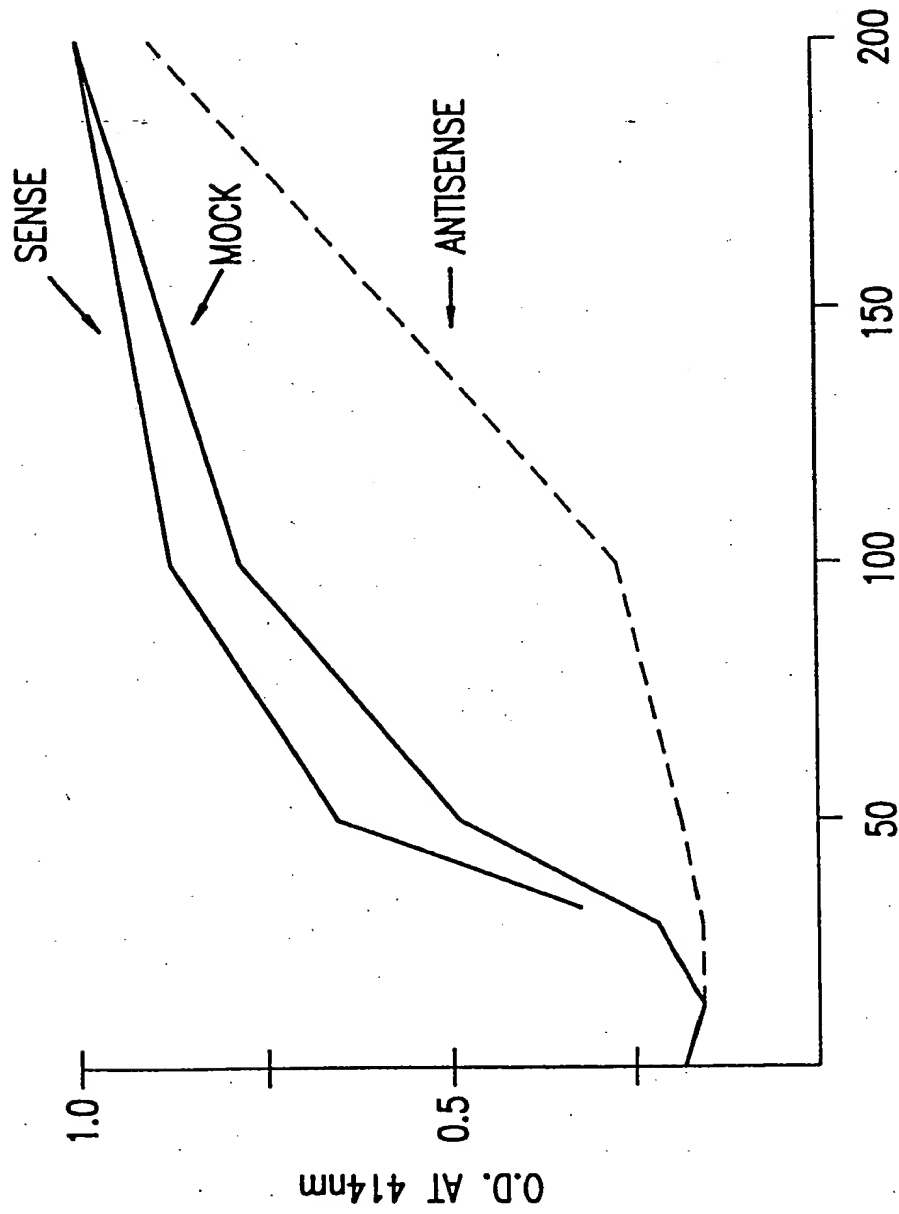


FIG. 6A

title: NOVEL MEGAKARYOCYTIC PROTEIN  
TYROSINE KINASES

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MKKI PROTEIN EXPRESSION

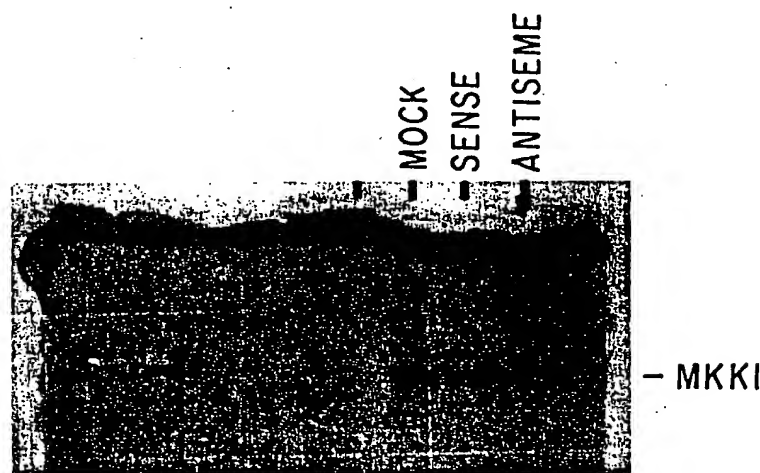


FIG. 6B

Title: NOVEL MEGAKARYOCYTIC PROTEIN

TYROSINE KINASES

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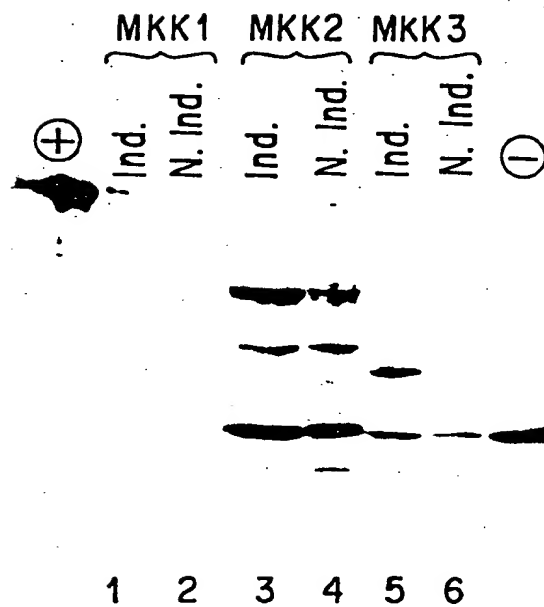


FIG. 7

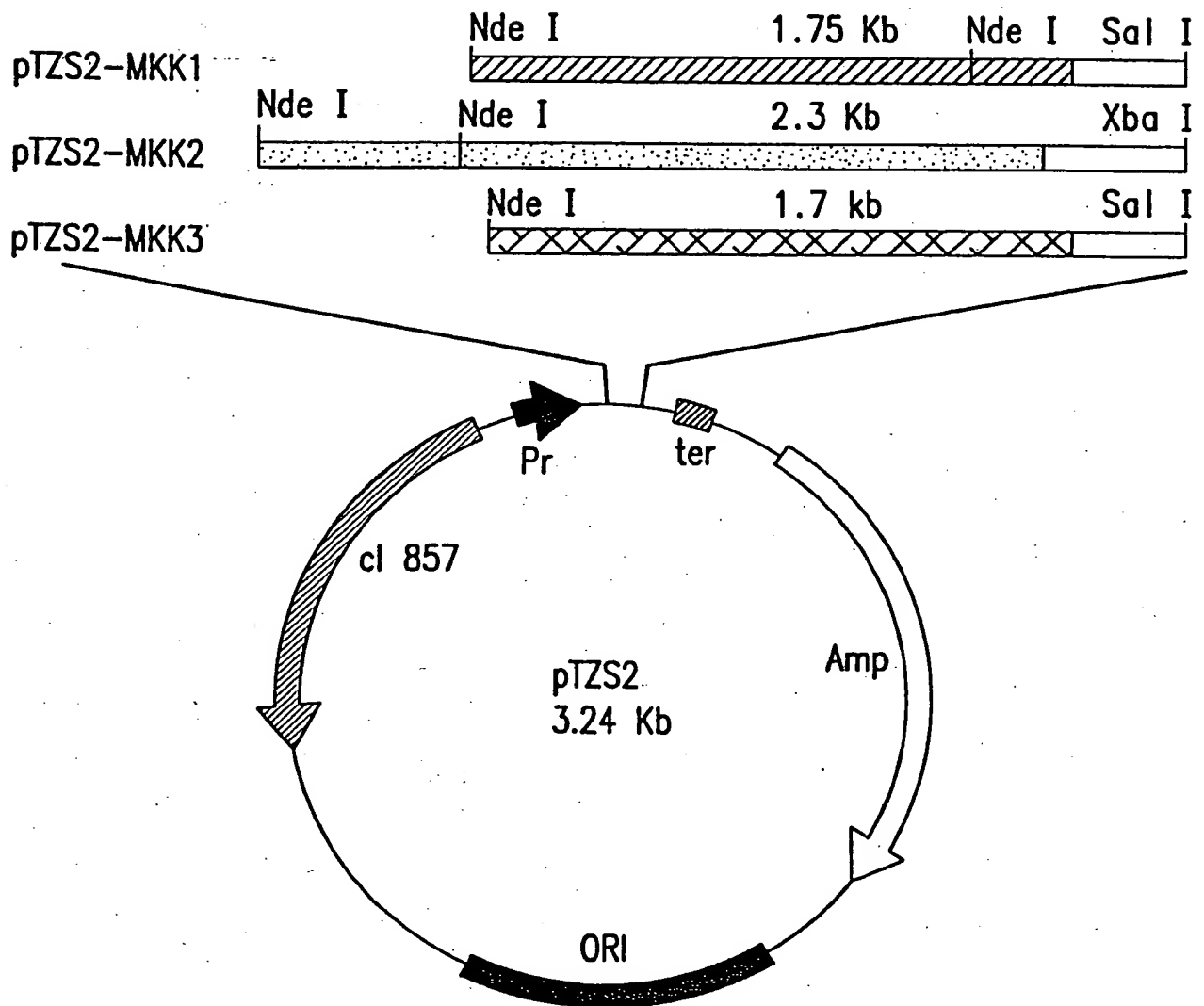


FIG.8

TYROSINE KINASES

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|     |   |               |
|-----|---|---------------|
| 1   | M A G R G S L V S W R A F H G C D S A E E L P R V S P R F L | MKK1 aa       |
| 1   | M S A I Q A A - - - - -                                     | hCSK (JH0559) |
| 31  | R A W H P P P V S A R M P T R R W A P G T O C I T K C E H T | MKK1 aa       |
| 8   | - - - - - W P S G T E C I A K Y N F H                       | hCSK (JH0559) |
| 61  | R P K P G E L A F R K G D V V T I L E A C E N K S W Y R V K | MKK1 aa       |
| 22  | G T A E Q D L P F C K G D V L T I V A V T K D P N W Y K A K | hCSK (JH0559) |
| 91  | H H T S G Q E G L L A A G A L R E R E A L S A D P K L S L M | MKK1 aa       |
| 52  | N K V - G R E G I I P A N Y V Q K R E G V K A G T K L S L M | hCSK (JH0559) |
| 121 | P W F H G K I S G Q E A V Q Q L O P P E D G L F L V R E S A | MKK1 aa       |
| 81  | P W F H G K I T R E Q A E R L L Y P P E T G L F L V R E S T | hCSK (JH0559) |
| 151 | R H P G D Y V L C V S F G R D V I H Y R V L H R D G H L T I | MKK1 aa       |
| 111 | N Y P G D Y T L C V S C D G K V E H Y R I M Y H A S K L S I | hCSK (JH0559) |
| 181 | D E A V F F C N L M D M V E H Y S K D K G A I C T K L V R P | MKK1 aa       |
| 141 | D E E V Y F E N L M Q L V E H Y T S D A D G L C T R L I K P | hCSK (JH0559) |
| 211 | K R K H G T K S A E E E L A R A G W L L N L Q H L T L G A Q | MKK1 aa       |
| 171 | K V M E G T V A A Q D E F Y R S G W A L N M K E L K L L Q T | hCSK (JH0559) |
| 241 | I G E G E F G A V L Q G E Y L G Q K V A V K N I K C D V T A | MKK1 aa       |
| 201 | I G K G E F G D V M L G D Y R G N K V A V K C I K N D A T A | hCSK (JH0559) |
| 271 | Q A F L D E T A V M T K M Q H E N L V R L L G V I L H Q - - | MKK1 aa       |
| 231 | Q A F L A E A S V M T Q L R H S N L V Q L L G V I V E E K G | hCSK (JH0559) |
| 299 | G L Y I V M E H V S K G N L V N F L R T R G R A L V N T A Q | MKK1 aa       |
| 261 | G L Y I V T E Y M A K G S L V D Y L R S R G R S V L G G D C | hCSK (JH0559) |
| 329 | L L Q F S L H V A E G M E Y L E S K K L V H R D L A A R N I | MKK1 aa       |
| 291 | L L K F S L D V C E A M E Y L E G N N F V H R D L A A R N V | hCSK (JH0559) |
| 359 | L V S E D L V A K V S D F G L A K A E R K G L D S S R L P V | MKK1 aa       |
| 321 | L V S E D N V A K V S D F G L T K E A S S T Q D T G K L P V | hCSK (JH0559) |

FIG.9A

Title: NOVEL MEGAKARYOCYTIC PROTEIN

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|     |   |               |
|-----|---|---------------|
| 389 | K W T A P E A L K H G K F T S K S D V W S F G V L L W E V F | MKK1 aa       |
| 351 | K W T A P E A L R E K K F S T K S D V W S F G I L L W E I Y | hCSK (JH0559) |
| 419 | S Y G R A P Y P K M S L K E V S E A V E K G Y R M E P P E G | MKK1 aa       |
| 381 | S F G R V P Y P R I P L K D V V P R V E K G Y K M D A P D G | hCSK (JH0559) |
| 449 | C P G P V H V L M S S C W E A E P A R R P P F R K L A E K L | MKK1 aa       |
| 411 | C P P A V Y E V M K N C W H L D A A M R P S F L Q L R E Q L | hCSK (JH0559) |
| 479 | A R E L R S A G A P A S V S G Q D A D G S T S P R S Q E P   | MKK1 aa       |
| 441 | E H - - - - - I K T H E L H - - - - - L                     | hCSK (JH0559) |

FIG.9B

NOVEL MEGAKARYOCYTIC PROTEIN

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|     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |      |          |          |         |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------|----------|----------|---------|
| 1   | M | D | T | K | S | I | L | E | E | L | L | K | R | S | Q | Q | K | K | K | M | S | P | N | N | Y | K | E | R | L | MKK2 | aa       |          |         |
| 1   | M | A | A | - | V | I | L | E | S | I | F | L | K | R | S | Q | Q | K | K | K | T | S | P | L | N | F | K | K | R | L    | hAlk     | (X58957) |         |
| 1   | M | N | N | F | I | L | L | E | E | Q | L | I | K | K | S | Q | Q | K | R | R | T | S | P | S | N | F | K | V | R | F    | hTKT     | (L10717) |         |
| 1   | M | M | V | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | -    | mTec     | (X5663)  |         |
| 31  | F | V | L | T | K | T | N | L | S | Y | Y | E | - | - | Y | D | K | M | K | R | G | S | R | K | G | S | I | E | I | K    | MKK2     | aa       |         |
| 30  | F | L | L | T | V | H | K | L | S | Y | Y | E | Y | D | F | E | R | G | R | G | S | K | K | G | S | I | D | V | E | hAlk | (X58957) |          |         |
| 31  | F | V | L | T | K | A | S | L | A | Y | F | E | D | R | - | - | H | G | K | K | R | T | L | K | G | S | I | E | L | S    | hTKT     | (L10717) |         |
| 4   | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | -    | mTec     | (X5663)  |         |
| 59  | K | I | R | C | V | E | K | V | N | L | E | E | Q | T | P | V | E | R | Q | - | - | - | - | - | - | - | - | - | - | -    | -        | MKK2     | aa      |
| 60  | K | I | T | C | V | E | T | V | V | P | E | K | N | P | P | P | E | R | Q | I | P | R | R | G | E | E | S | S | E | M    | hAlk     | (X58957) |         |
| 59  | R | I | K | C | V | E | I | V | K | S | D | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | -    | hTKT     | (L10717) |         |
| 4   | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | -    | mTec     | (X5663)  |         |
| 78  | - | - | - | - | - | - | - | - | - | - | - | Y | P | F | Q | I | V | Y | K | D | G | L | L | Y | V | Y | A | S | N | E    | E        | MKK2     | aa      |
| 90  | E | Q | I | S | I | I | E | R | F | P | Y | P | F | Q | V | V | Y | D | E | G | P | L | Y | V | F | S | P | T | E | E    | hAlk     | (X58957) |         |
| 70  | - | - | I | S | I | P | C | H | Y | K | Y | P | F | Q | V | V | H | D | N | Y | L | L | Y | V | F | A | P | D | R | E    | hTKT     | (L10717) |         |
| 4   | - | - | - | - | - | - | - | - | - | - | S | F | P | V | K | I | N | F | H | S | S | P | - | - | - | - | - | - | - | -    | Q        | mTec     | (X5663) |
| 98  | S | R | S | Q | W | L | K | A | L | Q | K | E | I | R | G | N | P | H | L | L | V | K | Y | H | S | G | F | F | V | D    | MKK2     | aa       |         |
| 120 | L | R | K | R | W | I | H | Q | L | K | N | V | I | R | Y | N | S | D | L | V | Q | K | Y | H | P | C | F | W | I | D    | hAlk     | (X58957) |         |
| 98  | S | R | Q | R | W | V | L | A | L | K | E | E | T | R | N | N | N | S | L | V | P | K | Y | H | P | N | F | W | M | D    | hTKT     | (L10717) |         |
| 17  | S | R | D | R | W | V | K | K | L | K | E | E | I | K | N | N | N | N | I | M | I | K | Y | H | P | K | F | W | A | D    | mTec     | (X5663)  |         |
| 128 | G | K | F | L | C | C | Q | Q | S | C | K | A | A | P | G | C | T | L | W | E | A | Y | A | N | L | H | T | A | V | N    | MKK2     | aa       |         |
| 150 | G | Q | Y | L | C | C | S | Q | T | A | K | N | A | M | G | C | Q | I | L | E | N | R | N | G | S | L | K | P | G | S    | hAlk     | (X58957) |         |
| 128 | G | K | W | R | C | C | S | Q | L | E | K | L | A | T | G | C | A | Q | Y | D | - | - | - | - | - | - | - | - | - | P    | hTKT     | (L10717) |         |
| 47  | G | S | Y | Q | C | C | R | Q | T | E | K | L | A | P | G | C | E | K | Y | N | L | F | E | S | S | I | - | - | - | -    | mTec     | (X5663)  |         |
| 158 | E | E | K | H | R | V | P | T | F | P | D | R | V | L | K | I | P | R | A | V | P | V | L | K | M | D | A | P | S | S    | MKK2     | aa       |         |
| 180 | S | H | R | K | T | K | K | P | L | P | P | - | - | - | - | T | P | E | E | D | Q | I | L | K | K | P | L | P | P | E    | hAlk     | (X58957) |         |
| 149 | T | K | N | A | S | K | K | P | L | P | P | - | - | - | - | T | P | E | D | N | R | - | - | - | - | - | - | - | - | hTKT | (L10717) |          |         |
| 73  | - | - | - | - | - | R | K | T | L | P | P | - | - | - | - | A | P | E | - | - | - | - | I | K | K | R | R | P | P | -    | mTec     | (X5663)  |         |
| 188 | S | T | T | L | A | Q | Y | D | N | E | S | K | K | N | Y | G | S | Q | P | P | S | S | S | T | S | L | A | Q | Y | D    | MKK2     | aa       |         |
| 206 | P | A | A | A | P | V | S | T | S | E | L | K | K | - | - | - | - | - | - | - | - | - | - | V | V | A | L | Y | D | hAlk | (X58957) |          |         |
| 166 | - | - | - | R | P | L | W | E | P | E | E | T | V | - | - | - | - | - | - | - | - | - | - | V | I | A | L | Y | D | hTKT | (L10717) |          |         |
| 89  | P | P | I | P | P | E | E | E | N | T | E | E | I | - | - | - | - | - | - | - | - | - | - | V | V | A | M | Y | D | mTEC | (X5663)  |          |         |

FIG.10A

## le: NOVEL MEGAKARYOCYTIC PROTEIN

## TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

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|     |   |      |          |
|-----|---|------|----------|
| 218 | S N S K K I Y G S Q P N F N M Q Y I P R E D F P - D W W Q V   | MKK2 | aa       |
| 225 | Y M P M N A N D L Q L R K G D E Y F I L E E S N L P W W R A   | hAkk | (X58957) |
| 182 | Y Q T N D P Q E L A L R R N E E Y C L L D S S E I H W W R V   | hTKT | (L10717) |
| 108 | F Q A T E A H D L R L E R G Q E Y I I L E K N D L H W W R A   | mTec | (X5663)  |
| 247 | R K L K S S S S S E D V A S S N Q K E R N V N H T T S K I S   | MKK2 | aa       |
| 255 | R D - - K N G Q E G Y I P S N Y V T E - A - - - - -           | hAkk | (X58957) |
| 212 | Q D - - R N G H E G Y V P S S Y L V E K S - - - - -           | hTKT | (L10717) |
| 138 | R D - - K -             | mTec | (X5663)  |
| 277 | W E F P E S S S S E E E E N L D D Y D W F A G N I S R S Q S   | MKK2 | aa       |
| 273 | - - - - - E D S I E M Y E W Y S K H M T R S Q A               | hAkk | (X58957) |
| 231 | - - - - - P N N L E T Y E W Y N K S I S R D K A               | hTKT | (L10717) |
| 141 | - - - - - Y G W Y C R N T N R S K A                           | mTec | (X5663)  |
| 307 | E Q L L R Q K G K E G A F M V R N S S Q V G M Y T V S L F S   | MKK2 | aa       |
| 292 | E Q L L K Q E G K E G G F I V R D S S K A G K Y T V S V F A   | hAkk | (X58957) |
| 250 | E K L L L D T G K E G A F M V R D S R T A G T Y T V S V F T   | hTKT | (L10717) |
| 154 | E Q L L R T E D K E G G F M V R D S S Q P G L Y T V S L Y T   | mTec | (X5663)  |
| 337 | K - A V N D K K G T V K H Y H V H - - T N A E N K L Y L A E   | MKK2 | aa       |
| 322 | K S T - G D P Q G V I R H Y V V - - C S T P Q S Q Y Y L A E   | hAkk | (X58957) |
| 280 | K A V V S E N N P C I K H Y H I K E T N D N P K R Y Y V A E   | hTKT | (L10717) |
| 184 | K F G - G E G S S G F R H Y H I K E T A T S P K K Y Y L A E   | mTec | (X5663)  |
| 364 | N Y C F D S I P K L I H Y H Q H N S A G M I T R L R H P V S   | MKK3 | aa       |
| 349 | K H L F S T I P E L I N Y H Q H N S A G L I S R L K Y P V S   | hAkk | (X58957) |
| 310 | K Y V F D S I P L L I N Y H Q H N G G G L V T R L R Y P V C   | hTKT | (L10717) |
| 213 | K H A F G S I P E T I I E Y H K H N A A G L V T R L R Y P V S | mTec | (X5663)  |
| 394 | T K A N K V P D S V S L G N G I W E L K R E E I T L L K E L   | MKK2 | aa       |
| 379 | Q Q N K N A P S T A G L G Y G S W E I D P K D L T F L K E L   | hAkk | (X58957) |
| 340 | F G R Q K A P V T A G L R Y G K W V I D P S E L T F V Q E I   | hTKT | (L10717) |
| 243 | T K G K N A P T T A G F S Y D K W E I N P S E L T F M R E L   | mTec | (X5663)  |
| 424 | G S G Q F G V V Q L G K W K G Q Y D V A V K M I K E G S M S   | MKK2 | aa       |
| 409 | G T G Q F G V V K Y G K W R G Q Y D V A I K M I K E G S M S   | hAkk | (X58957) |
| 370 | G S G Q F G L V H L G Y W L N K D K V A I K T I R E G A M S   | hTKT | (L10717) |
| 273 | G S G L F G V V R L G K W R A Q Y K V A I K A I R E G A M C   | mTec | (X5663)  |

FIG.10B



TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

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|     |   |       |          |
|-----|---|-------|----------|
| 454 | E D E F F Q E A Q T M M K L S H P K L V K F Y G V C S K E Y | MKK2  | aa       |
| 439 | E D E F I E E A K V M M N L S H E K L V Q L Y G V C T K Q R | hA tk | (X58957) |
| 400 | E E D F I E E A E V M M K L S H P K L V Q L Y G V C L E Q A | hTKT  | (L10717) |
| 303 | E E D F I E E A K V M M K L T H P K L V Q L Y G V C T Q Q K | mTec  | (X5663)  |
| 484 | P I Y I V T E Y I S N G C L L N Y L R S H G K G L E P S Q L | MKK2  | aa       |
| 469 | P I F I I T E Y M A N G C L L N Y L R E M R H R F Q T Q Q L | hA tk | (X58957) |
| 430 | P I C L V F E F M E H G C L S D Y L R T Q R G L F A A E T L | hTKT  | (L10717) |
| 333 | P I Y I V T E F M E R G C L L N F L R Q R Q G H F S R D M L | mTec  | (X5663)  |
| 514 | L E M C Y D V C E G M A F L E S H Q F I H R D L A A R N C L | MKK2  | aa       |
| 499 | L E M C K D V C E A M E Y L E S K Q F L H R D L A A R N C L | hA tk | (X58957) |
| 460 | L G M C L D V C E G M A Y L E E A C V I H R D L A A R N C L | hTKT  | (L10717) |
| 363 | L S M C Q D V C E G M E Y L E R N S F I H R D L A A R N C L | mTec  | (X5663)  |
| 544 | V D R D L C V K V S D F G M T R Y V L D D Q Y V S S V G T K | MKK2  | aa       |
| 529 | V N D Q G V V K V S D F G L S R Y V L D D E Y T S S V G S K | hA tk | (X58957) |
| 490 | V G E N Q V I K V S D F G M T R F V L D D Q Y T S S T G T K | hTKT  | (L10717) |
| 393 | V N E A G V V K V S D F G M A R Y V L D D Q Y T S S S G A K | mTec  | (X5663)  |
| 574 | F P V K W S A P E V F H Y F K Y S S K S D V W A F G I L M W | MKK2  | aa       |
| 559 | F P V R W S P P E V L M Y S K F S S K S D I W A F G V L M W | hA tk | (X58957) |
| 520 | F P V K W A S P E V F S F S R Y S S K S D V W S F G V L M W | hTKT  | (L10717) |
| 423 | F P V K W C P P E V F N Y S R F S S K S D V W S F G V L M W | mTec  | (X5663)  |
| 604 | E V F S L G K Q P Y D L Y D N S Q V V L K V S Q G H R L Y R | MKK2  | aa       |
| 589 | E I Y S L G K M P Y E R F T N S E T A E H I A Q G L R L Y R | hA tk | (X58957) |
| 550 | E V F S E G K I P Y E N R S N S E V V E D I S T G F R L Y K | hTKT  | (L10717) |
| 453 | E I F T E G R M P F E K N T N Y E V V T M V T R G H R L H R | mTec  | (X5663)  |
| 634 | P H L A S D T I Y Q I M Y S C W H E L P E K R P T F Q Q L L | MKK2  | aa       |
| 619 | P H L A S E K V Y T I M Y S C W H E K A D E R P T F K I L L | hA tk | (X58957) |
| 580 | P R L A S T H V Y Q I M N H C W K E R P E D R P A F S R L L | hTKT  | (L10717) |
| 483 | P K L A T K Y L Y E V M L R C W Q E R P E G R P S F E D L L | mTec  | (X5663)  |
| 664 | S S I E P L R E K D K H                                     | MKK2  | aa       |
| 649 | S N I L D V M D E E S                                       | hA tk | (X58957) |
| 610 | R Q L A E I A E S - - - - G L                               | hTKT  | (L10717) |
| 513 | R T I D E L V E C E E T F G R                               | mTec  | (X5663)  |

FIG.10C

FIG. 11A

|     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |             |      |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|-------------|------|
| 69  | L | Q | V | L | D | T | L | H | E | G | W | W | F | A | R | H | L | E | K | R | R | D | G | S | S | Q | Q | L | Q | G | MKK3 MPI aa |      |
| 109 | F | Q | I | L | N | S | S | E | G | D | W | W | E | A | R | S | L | T | T | G | E | T | G | - | - | - | - | - | - | - | -           | hFyn |
| 108 | F | H | I | I | N | N | T | E | G | D | W | W | E | A | R | S | L | S | S | G | A | T | G | - | - | - | - | - | - | - | -           | cYrk |
| 111 | L | Q | I | V | N | N | T | E | G | D | W | W | L | A | H | S | L | S | T | G | Q | T | G | - | - | - | - | - | - | - | -           | hSrc |
| 118 | F | Q | I | I | N | N | T | E | G | D | W | W | E | A | R | S | I | A | T | G | K | N | G | - | - | - | - | - | - | - | -           | hYes |
| 104 | F | H | I | L | N | N | T | E | G | D | W | W | E | A | R | S | L | S | S | G | K | T | G | - | - | - | - | - | - | - | -           | hFgr |
| 90  | M | K | V | L | E | E | H | - | G | E | W | W | K | A | K | S | L | L | T | K | K | E | G | - | - | - | - | - | - | - | -           | hLyn |
| 84  | M | V | V | L | E | E | S | - | G | E | W | W | K | A | R | S | L | A | T | R | K | E | G | - | - | - | - | - | - | - | -           | hHck |
| 88  | L | R | I | L | E | Q | S | - | G | E | W | W | K | A | Q | S | L | T | T | G | Q | E | G | - | - | - | - | - | - | - | -           | hLck |
| 79  | L | Q | V | L | R | S | T | - | G | D | W | W | L | A | R | S | L | V | T | G | R | E | G | - | - | - | - | - | - | - | -           | mBik |
| 99  | Y | I | P | S | N | Y | V | A | E | D | R | S | L | Q | A | E | P | W | F | F | G | A | I | G | R | S | D | A | E | K | MKK3 MPI aa |      |
| 132 | Y | I | P | S | N | Y | V | A | P | V | D | S | I | Q | A | E | E | W | Y | F | G | K | L | G | R | K | D | A | E | R | hFyn        |      |
| 131 | Y | I | P | S | N | Y | V | A | P | V | D | S | I | Q | A | E | E | W | Y | F | G | K | I | G | R | K | D | A | E | R | cYrk        |      |
| 134 | Y | I | P | S | N | Y | V | A | P | S | D | S | I | Q | A | E | E | W | Y | F | G | K | I | T | R | R | E | S | E | R | hSrc        |      |
| 141 | Y | I | P | S | N | Y | V | A | P | A | D | S | I | Q | A | E | E | W | Y | F | G | K | M | G | R | K | D | A | E | R | hYes        |      |
| 127 | C | I | P | S | N | Y | V | A | P | V | D | S | I | Q | A | E | E | W | Y | F | G | K | I | G | R | K | D | A | E | R | hFgr        |      |
| 112 | F | I | P | S | N | Y | V | A | K | L | N | T | L | E | T | E | E | W | F | F | K | D | I | T | R | K | D | A | E | R | hLyn        |      |
| 106 | Y | I | P | S | N | Y | V | A | R | V | D | S | L | E | T | E | E | W | F | F | K | G | I | S | R | K | D | A | E | R | hHck        |      |
| 110 | F | I | P | F | N | F | V | A | K | A | N | S | L | E | P | E | P | W | F | F | K | N | L | S | R | K | D | A | E | R | hLck        |      |
| 101 | Y | V | P | S | N | F | V | A | P | V | E | T | L | E | V | E | K | W | F | F | R | T | I | S | R | K | D | A | E | R | mBik        |      |
| 129 | Q | L | L | Y | S | E | N | K | T | G | S | F | L | I | R | E | S | E | S | Q | K | G | E | F | S | L | S | V | L | D | MKK3 MPI aa |      |
| 162 | Q | L | L | S | F | G | N | P | R | G | T | F | L | I | R | E | S | E | T | T | K | G | A | Y | S | L | S | I | R | D | hFyn        |      |
| 161 | Q | L | L | C | H | G | N | C | R | G | T | F | L | I | R | E | S | E | T | T | K | G | A | Y | S | L | S | I | R | D | cYrk        |      |
| 164 | L | L | L | N | A | E | N | P | R | G | T | F | L | V | R | E | S | E | T | T | K | G | A | Y | C | L | S | V | S | D | hSrc        |      |
| 171 | L | L | L | N | P | G | N | Q | R | G | I | F | L | V | R | E | S | E | T | T | K | G | A | Y | S | L | S | I | R | D | hYes        |      |
| 157 | Q | L | L | S | P | G | N | P | Q | G | A | F | L | I | R | E | S | E | T | T | K | G | A | Y | S | L | S | I | R | D | hLyn        |      |
| 142 | Q | L | L | A | P | G | N | S | A | G | A | F | L | I | R | E | S | E | T | L | K | G | S | F | S | L | S | V | R | D | hHck        |      |
| 136 | Q | L | L | A | P | G | N | M | L | G | S | F | M | I | R | D | S | E | T | T | K | G | S | Y | S | L | S | V | R | D | hHck        |      |
| 140 | Q | L | L | A | P | G | N | T | H | G | S | F | L | I | R | E | S | E | S | T | A | G | S | F | S | L | S | V | R | D | hLck        |      |
| 131 | Q | L | L | A | P | M | N | K | A | G | S | F | L | I | R | E | S | E | S | N | K | G | A | F | S | L | S | V | K | D | mBik        |      |
| 159 | - | - | - | - | - | G | A | V | V | K | H | Y | R | I | K | R | L | D | E | G | G | F | F | L | T | R | R | R | I | F | MKK3 MPI aa |      |
| 192 | W | D | D | M | K | G | D | H | V | K | H | Y | K | I | R | K | L | D | N | G | G | Y | Y | I | T | T | R | A | Q | F | hFyn        |      |
| 191 | W | D | E | A | K | G | D | H | V | K | H | Y | K | I | R | K | L | D | S | G | G | Y | Y | I | T | T | R | A | Q | F | cYrk        |      |
| 194 | F | D | N | A | K | G | L | N | V | K | H | Y | K | I | R | K | L | D | S | G | G | F | Y | I | T | S | R | T | Q | F | hSrc        |      |
| 201 | W | D | E | I | R | G | D | N | V | K | H | Y | K | I | R | K | L | D | N | G | G | Y | Y | I | T | T | R | A | Q | F | hYes        |      |
| 187 | W | D | Q | T | R | G | D | H | V | K | H | Y | K | I | R | K | L | D | M | G | G | Y | Y | I | T | T | R | V | Q | F | hFgr        |      |
| 172 | F | D | P | V | H | G | D | V | I | K | H | Y | K | I | R | S | L | D | N | G | G | Y | Y | I | S | P | R | I | T | F | hLyn        |      |
| 166 | Y | D | P | R | Q | G | D | T | V | K | H | Y | K | I | R | T | L | D | N | G | G | F | Y | I | S | P | R | S | T | F | hHck        |      |
| 170 | F | D | Q | N | Q | G | E | V | V | K | H | Y | K | I | R | N | L | D | N | G | G | F | Y | I | S | P | R | I | T | F | hLck        |      |
| 161 | I | T | T | - | Q | G | E | V | V | K | H | Y | K | I | R | S | L | D | N | G | G | Y | Y | I | S | P | R | I | T | F | mBik        |      |

FIG.11B

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

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|     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |          |    |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|----------|----|
| 184 | S | T | L | N | E | F | V | S | H | Y | T | K | T | S | D | G | L | C | V | K | L | G | K | P | C | L | K | I | Q | V | MKK3 MPI | aa |
| 222 | E | T | L | Q | Q | L | V | Q | H | Y | S | E | R | A | A | G | L | C | C | R | L | V | V | P | C | H | K | G | M | - | hFyn     |    |
| 221 | D | T | I | Q | Q | L | V | Q | H | Y | I | E | R | A | A | G | L | C | C | R | L | A | V | P | C | P | K | G | T | - | cYrk     |    |
| 224 | N | S | L | Q | Q | L | V | A | Y | Y | S | K | H | A | D | G | L | C | H | R | L | T | T | V | C | P | T | S | K | - | hSrc     |    |
| 231 | D | T | L | Q | K | L | V | K | H | Y | T | E | H | A | D | G | L | C | H | K | L | T | T | V | C | P | T | V | K | - | hYes     |    |
| 217 | N | S | V | Q | E | L | V | Q | H | Y | M | E | V | N | D | G | L | C | N | L | L | I | A | P | C | T | I | M | K | - | hFgr     |    |
| 202 | P | C | I | S | D | M | I | K | H | Y | Q | K | Q | A | D | G | L | C | R | R | L | E | K | A | C | I | S | P | K | - | hLyn     |    |
| 196 | S | T | L | Q | E | L | V | D | H | Y | K | K | G | N | D | G | L | C | Q | K | L | S | V | P | C | M | S | S | K | - | hHck     |    |
| 200 | P | G | L | H | E | L | V | R | H | Y | T | N | A | S | D | G | L | C | T | R | L | S | R | P | C | Q | T | Q | K | - | hLck     |    |
| 190 | P | T | L | Q | A | L | V | Q | H | Y | S | K | K | G | D | G | L | C | Q | K | L | T | L | P | C | V | N | L | A | - | mBik     |    |
| 214 | P | A | P | F | D | L | S | Y | K | T | V | D | Q | W | E | I | D | R | N | S | I | Q | L | L | K | R | L | G | S | G | MKK3 MPI | aa |
| 251 | P | R | L | T | D | L | S | V | K | T | K | D | V | W | E | I | P | R | E | S | L | Q | L | I | K | R | L | G | N | G | hFyn     |    |
| 250 | P | K | L | A | D | L | S | V | K | T | K | D | V | W | E | I | P | R | E | S | L | Q | L | L | Q | K | L | G | N | G | cYrk     |    |
| 253 | P | Q | T | Q | G | L | A | - | - | - | K | D | A | W | E | I | P | R | E | S | L | R | L | E | V | K | L | G | Q | G | hSrc     |    |
| 260 | P | Q | T | Q | G | L | A | - | - | - | K | D | A | W | E | I | P | R | E | S | L | R | L | E | V | K | L | G | Q | G | hYes     |    |
| 246 | P | Q | T | L | G | L | A | - | - | - | K | D | A | W | E | I | S | R | S | S | I | T | L | E | R | R | L | G | T | G | hFgr     |    |
| 231 | P | Q | - | - | - | - | K | P | W | D | K | D | A | W | E | I | P | R | E | S | I | K | L | V | K | R | L | G | A | G | hLyn     |    |
| 225 | P | Q | - | - | - | - | K | P | W | E | K | D | A | W | E | I | P | R | E | S | L | K | L | E | K | K | L | G | A | G | hHck     |    |
| 229 | P | Q | - | - | - | - | K | P | W | W | E | D | E | W | E | V | P | R | E | T | L | K | L | V | E | R | L | G | A | G | hLck     |    |
| 219 | P | K | - | - | - | - | N | L | W | A | Q | D | E | W | E | I | P | R | Q | S | L | K | L | V | R | K | L | G | S | G | mBik     |    |
| 244 | Q | F | G | E | V | W | E | G | L | W | N | N | T | T | P | V | A | V | K | T | L | K | P | G | S | M | D | P | N | D | MKK3 MPI | aa |
| 281 | Q | F | G | E | V | W | M | G | T | W | N | G | N | T | K | V | A | I | K | T | L | K | P | G | T | M | S | P | E | S | hFyn     |    |
| 280 | Q | F | G | E | V | W | M | G | T | W | N | G | T | T | K | V | A | V | K | T | L | K | P | G | T | M | S | P | E | A | cYrk     |    |
| 280 | C | F | G | E | V | W | M | G | T | W | N | G | T | T | R | V | A | I | K | T | L | K | P | G | T | M | S | P | E | A | hSrc     |    |
| 287 | C | F | G | E | V | W | M | G | T | W | N | G | T | T | K | V | A | I | K | T | L | K | P | G | T | M | M | P | E | A | hYES     |    |
| 273 | C | F | G | D | V | W | L | G | T | W | N | G | S | T | K | V | A | V | K | T | L | K | P | G | T | M | S | P | K | A | hFgr     |    |
| 257 | Q | F | G | E | V | W | M | G | Y | Y | N | N | S | T | K | V | A | V | K | T | L | K | P | G | T | M | S | V | Q | A | hLyn     |    |
| 251 | Q | F | G | E | V | W | M | A | T | Y | N | K | H | T | K | V | A | V | K | T | M | K | P | G | S | M | S | V | E | A | hHck     |    |
| 255 | Q | F | G | E | V | W | M | G | Y | Y | N | G | H | T | K | V | A | V | K | S | L | K | Q | G | S | M | S | P | D | A | hLck     |    |
| 245 | Q | F | G | E | V | W | M | G | Y | Y | K | N | N | M | K | V | A | T | K | T | L | K | E | G | T | M | S | P | E | A | mBik     |    |
| 274 | F | L | R | E | A | Q | I | M | K | N | L | R | H | P | K | L | I | Q | L | Y | A | V | C | T | L | E | D | P | I | Y | MKK3 MPI | aa |
| 311 | F | L | E | E | A | Q | I | M | K | K | L | K | H | D | K | L | V | Q | L | Y | A | V | V | S | - | E | E | P | I | Y | hFyn     |    |
| 310 | F | L | E | E | A | Q | I | M | K | R | L | R | H | D | K | L | V | Q | L | Y | A | V | V | S | - | E | E | P | I | Y | cYrk     |    |
| 310 | F | L | Q | E | A | Q | V | M | K | K | L | R | H | E | K | L | V | Q | L | Y | A | V | V | S | - | E | E | P | I | Y | hSrc     |    |
| 317 | F | L | Q | E | A | Q | I | M | K | K | L | R | H | D | K | L | V | P | L | Y | A | V | V | S | - | E | E | P | I | Y | hYes     |    |
| 303 | F | L | E | E | A | Q | V | M | K | L | L | R | H | D | K | L | V | Q | L | Y | A | V | V | S | - | E | E | P | I | Y | hFgr     |    |
| 287 | F | L | E | E | A | N | L | M | K | T | L | Q | H | D | K | L | V | R | L | Y | A | V | V | T | R | E | E | P | I | Y | hLyn     |    |
| 281 | F | L | A | E | A | N | V | M | K | T | L | Q | H | D | K | L | V | K | L | H | A | V | V | T | K | E | - | P | I | Y | hHck     |    |
| 285 | F | L | A | E | A | N | L | M | K | Q | L | Q | H | Q | R | L | V | R | L | Y | A | V | V | T | - | Q | E | P | I | Y | hLck     |    |
| 275 | F | L | G | E | A | N | V | M | K | T | L | Q | H | E | R | L | V | R | L | Y | A | V | V | T | R | E | - | P | I | Y | mBik     |    |

FIG.11C

## TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

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|     |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |   |      |          |    |          |    |
|-----|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|------|----------|----|----------|----|
| 304 | I | L | T | E | L | M | R | H | G | S | L | Q | E | Y | L | Q | N | D | T | G | S | K | I | H | L | T | Q | Q | V | D    | MKK3 MPI | oo |          |    |
| 340 | I | V | T | E | Y | M | N | K | G | S | L | L | D | F | L | K | D | G | E | G | R | A | L | K | L | P | N | L | V | D    | hFyn     |    |          |    |
| 339 | I | V | T | E | F | M | S | Q | G | S | L | L | D | F | L | K | D | G | D | G | R | Y | L | K | L | P | Q | L | V | D    | cYrk     |    |          |    |
| 339 | I | V | T | E | Y | M | S | K | G | S | L | L | D | F | L | K | G | E | T | G | K | Y | L | R | L | P | Q | L | V | D    | hSrc     |    |          |    |
| 346 | I | V | T | E | F | M | S | K | G | S | L | L | D | F | L | K | E | G | D | G | K | Y | L | K | L | P | Q | L | V | D    | hYes     |    |          |    |
| 332 | I | V | T | E | F | M | C | H | G | S | L | L | D | F | L | K | N | P | E | G | Q | D | L | R | L | P | Q | L | V | D    | hFgr     |    |          |    |
| 317 | I | I | T | E | Y | M | A | K | G | S | L | L | D | F | L | K | S | D | E | G | G | K | V | L | L | P | K | L | I | D    | hLyn     |    |          |    |
| 310 | I | I | T | E | F | M | A | K | G | S | L | L | D | F | L | K | S | D | E | G | S | K | Q | P | L | P | K | L | I | D    | hHck     |    |          |    |
| 314 | I | I | T | E | Y | M | E | N | G | S | L | V | D | F | L | K | T | P | S | G | I | K | L | T | I | N | K | L | L | D    | hLck     |    |          |    |
| 304 | I | V | T | E | Y | M | A | R | G | C | L | L | D | F | L | K | T | D | E | G | S | R | L | S | L | P | R | L | I | D    | mBik     |    |          |    |
| 334 | M | A | A | Q | V | A | S | G | M | A | Y | L | E | S | R | N | Y | I | H | R | D | L | A | A | R | N | V | L | V | G    | MKK3 MPI | oo |          |    |
| 370 | M | A | A | Q | V | A | A | G | M | A | Y | I | E | R | M | N | U | I | H | R | D | L | R | S | A | N | I | L | V | G    | hFyn     |    |          |    |
| 369 | M | A | A | Q | I | A | A | G | M | A | Y | I | E | R | M | N | Y | I | H | R | D | L | R | A | A | N | I | L | V | G    | cYrk     |    |          |    |
| 369 | M | A | A | Q | I | A | S | G | M | A | Y | V | E | R | M | N | Y | V | H | R | D | L | R | A | A | N | I | L | V | G    | hSrc     |    |          |    |
| 376 | M | A | A | Q | I | A | D | G | M | A | Y | I | E | R | M | N | Y | I | H | R | D | L | R | A | A | N | I | L | V | G    | hYes     |    |          |    |
| 362 | M | A | A | Q | V | A | E | G | M | A | Y | M | E | R | M | N | Y | I | H | R | D | L | R | A | A | N | I | L | V | G    | hFgr     |    |          |    |
| 347 | F | S | A | Q | I | A | E | G | M | A | Y | I | E | R | K | N | Y | I | H | R | D | L | R | A | A | N | V | L | V | S    | hLyn     |    |          |    |
| 340 | F | S | A | Q | I | A | E | G | M | A | F | I | E | Q | R | N | Y | I | H | R | D | L | R | A | A | N | I | L | V | S    | hHck     |    |          |    |
| 344 | M | A | A | Q | I | A | E | G | M | A | F | I | E | E | R | N | Y | I | H | R | D | L | R | A | A | N | I | L | V | S    | hLck     |    |          |    |
| 334 | M | S | A | Q | V | A | E | G | M | A | Y | I | E | R | M | N | S | I | H | R | D | L | R | A | A | N | I | L | V | S    | mBik     |    |          |    |
| 364 | E | H | N | I | Y | K | V | A | D | F | G | L | A | R | L | I | V | F | K | V | D | N | E | D | I | Y | E | S | R | H    | E        | I  | MKK3 MPI | oo |
| 400 | N | G | L | I | C | K | I | A | D | F | G | L | A | R | L | I | - | - | - | E | D | N | E | Y | T | A | R | Q | G | A    | hFyn     |    |          |    |
| 399 | D | N | L | V | C | K | I | A | D | F | G | L | A | R | L | I | - | - | - | E | D | N | E | Y | T | A | R | Q | G | A    | cYrk     |    |          |    |
| 399 | E | N | L | V | C | K | V | A | D | F | G | L | A | R | L | I | - | - | - | E | D | N | E | Y | T | A | R | Q | G | A    | hSrc     |    |          |    |
| 406 | E | N | L | V | C | K | I | A | D | F | G | L | A | R | L | I | - | - | - | E | D | N | E | Y | T | A | R | Q | G | A    | hYes     |    |          |    |
| 392 | E | R | L | A | C | K | I | A | D | F | G | L | A | R | L | I | - | - | - | K | D | D | E | Y | N | P | C | Q | G | S    | hFgr     |    |          |    |
| 377 | E | S | L | M | C | K | I | A | D | F | G | L | A | R | V | I | - | - | - | E | D | N | E | Y | T | A | R | E | G | A    | hLyn     |    |          |    |
| 370 | A | S | L | V | C | K | I | A | D | F | G | L | A | R | V | I | - | - | - | E | D | N | E | Y | T | A | R | E | G | A    | hHck     |    |          |    |
| 374 | D | T | L | S | C | K | I | A | D | F | G | L | A | R | L | I | - | - | - | E | D | N | E | Y | T | A | R | E | G | A    | hLck     |    |          |    |
| 364 | E | T | L | C | C | K | I | A | D | F | G | L | A | R | I | I | - | - | - | D | S | E | Y | T | A | Q | E | G | A | mBik |          |    |          |    |
| 394 | K | L | P | V | K | W | T | A | P | E | A | I | R | S | N | K | F | S | I | K | S | D | V | W | S | F | G | I | L | L    | MKK3 MPI | oo |          |    |
| 427 | K | F | P | I | K | W | T | A | P | E | A | A | L | Y | G | R | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | hFyn     |    |          |    |
| 426 | K | F | P | I | K | W | T | A | P | E | A | A | L | F | G | K | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | cYrk     |    |          |    |
| 426 | K | F | P | I | K | W | T | A | P | E | A | A | L | Y | G | R | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | hSrc     |    |          |    |
| 433 | K | F | P | I | K | W | T | A | P | E | A | A | L | Y | G | R | F | T | I | K | S | D | V | W | S | F | G | I | L | Q    | hYes     |    |          |    |
| 419 | K | F | P | I | K | W | T | A | P | E | A | A | L | F | G | R | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | hFgr     |    |          |    |
| 404 | K | F | P | I | K | W | T | A | P | E | A | I | N | F | G | C | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | hLyn     |    |          |    |
| 397 | K | F | P | I | K | W | T | A | P | E | A | I | N | F | G | S | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | hHck     |    |          |    |
| 401 | K | F | P | I | K | W | T | A | P | E | A | I | N | Y | G | T | F | T | I | K | S | D | V | W | S | F | G | I | L | L    | hLck     |    |          |    |
| 390 | K | F | P | I | K | W | T | A | P | E | A | I | H | F | G | V | F | T | I | K | A | D | V | W | S | F | G | V | L | L    | mBik     |    |          |    |

FIG.11D

## TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

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|     |   |             |
|-----|---|-------------|
| 424 | Y E I I T Y G K M P Y S G M T G A Q V I Q M L A Q N Y R L P | MKK3 MPI aa |
| 457 | T E L V T K G R V P Y P G M N N R E V L E Q V E R G Y R M P | hFyn        |
| 456 | T E L V T K G R V P Y P G M N N R E V L E Q V E R G Y R M Q | cYrk        |
| 456 | T E L T T K G R V P Y P G M V N R E V L D Q V E R G Y R M P | hSrc        |
| 463 | T E L V T K G R V P Y P G M V N R E V L E Q V E R G Y R M P | hYes        |
| 449 | T E L I T K G R I P Y P G M N K R E V L E Q V E Q G Y H M P | hFgr        |
| 434 | Y E I V T Y G K I P Y P G R T N A D V M T A L S Q G Y R M P | hLyn        |
| 427 | M E I V T Y G R I P Y P G M S N P E V I R A L E R G Y R M P | hHck        |
| 431 | T E I V T H G R I P Y P G M T N P E V I Q N L E R G Y R M V | hLck        |
| 420 | M V I V T Y G R V P Y P G M S N P E V I R S L E H G Y R M P | mBik        |
| 454 | Q P S N C P Q Q F Y N - I M L E C W N A E P K E R P T F E T | MKK3 MPI aa |
| 487 | C P Q D C P I S L H - E L M I H C W K K D P E E R P T F E Y | hFyn        |
| 486 | C P G G C P P S L H - D V M V Q C W K R E P E E R P T F E Y | cYrk        |
| 486 | C P P E C P E S L H - D L M C Q C W R K E P E E R P T F E Y | hSrc        |
| 493 | C P Q G C P E S L H - E L M N L C W K K D P D E R P T F E Y | hYes        |
| 479 | C P P G C P A S L Y - E A M E Q T W R L D P E E R P T F E Y | hFgr        |
| 464 | R V E N C P D E L Y - D I M K M C W K E K A E E R P T F D Y | hLyn        |
| 457 | R P E N C P E E L Y - N I M M R C W K N R P E E R P T F E Y | hHck        |
| 461 | R P D N C P E E L Y - Q L M R L C W K E R P E D R P T F D Y | hLck        |
| 450 | C P E T C P P E L Y N D I I T E C W R G R P E E R P T F E F | mBik        |
| 483 | L R W K L E D Y F E - T D S S Y S D A N N F I R             | MKK3 MPI aa |
| 516 | L Q S F L E D Y F T A T E P Q Y Q P G E N - - - L           | hFyn        |
| 515 | L Q S F L E D Y F T A T E P Q Y Q P G D N - - - Q           | cYrk        |
| 515 | L Q A F L E D Y F T S T E P Q Y Q P G E N - - - L           | hSrc        |
| 522 | I Q S F L E D Y F T A T E P Q Y Q P G E N - - - L           | hYes        |
| 508 | L Q S F L E D Y F T S A E P Q Y Q P G D Q - - - T           | hFgr        |
| 493 | L Q S V L D D F Y T A T E G Q Y Q Q - - Q - - - P           | hLyn        |
| 486 | I Q S V L D D F Y T A T E S Q Y Q Q - - Q - - - P           | hHck        |
| 490 | L R S V L E D F F T A T E G Q Y Q P - - Q - - - P           | hLck        |
| 480 | L Q S V L E D F Y T A T E G Q Y E L - - Q - - - P           | mBik        |

FIG.11E

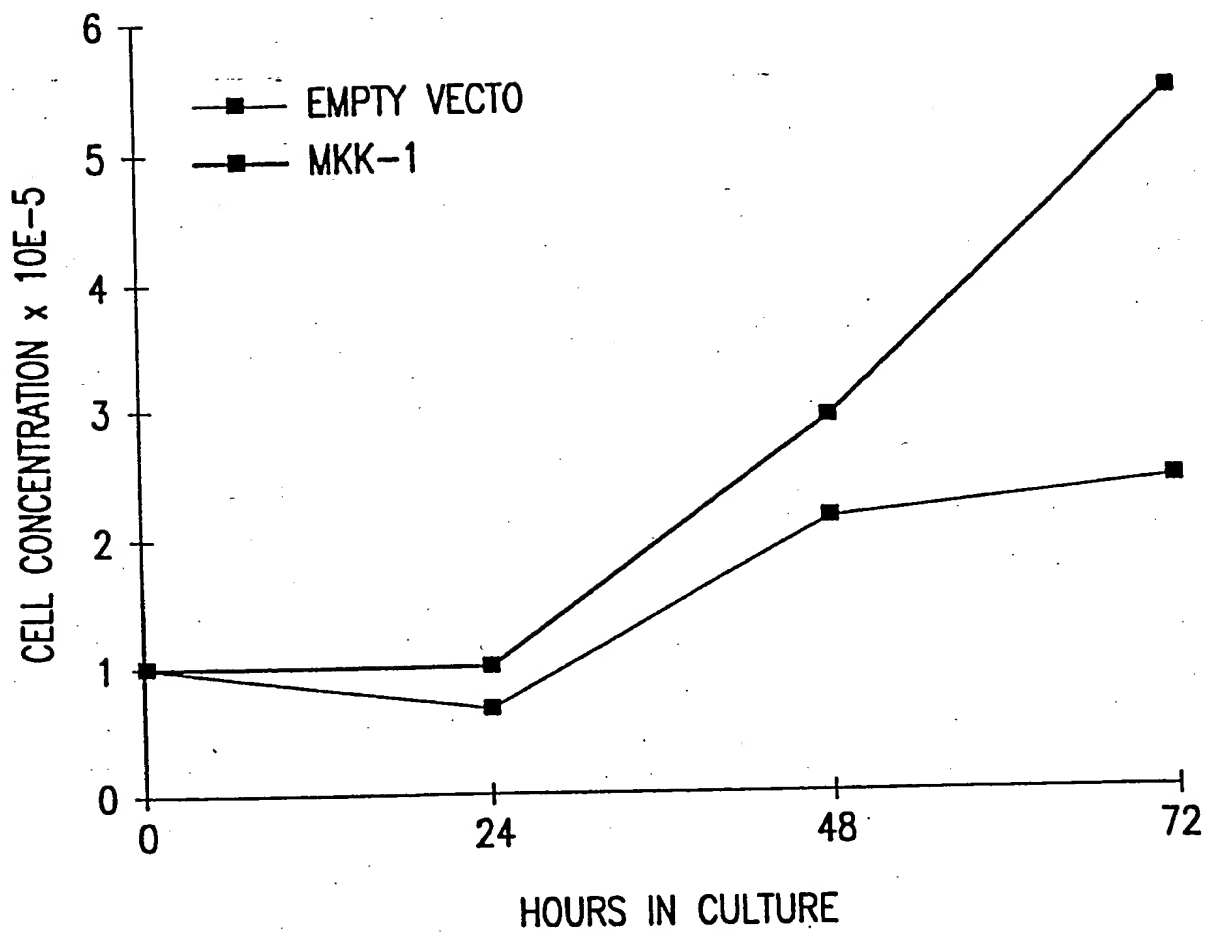


FIG.12

TYROSINE KINASES

Inventor(s): Axel ULLRICH et al.

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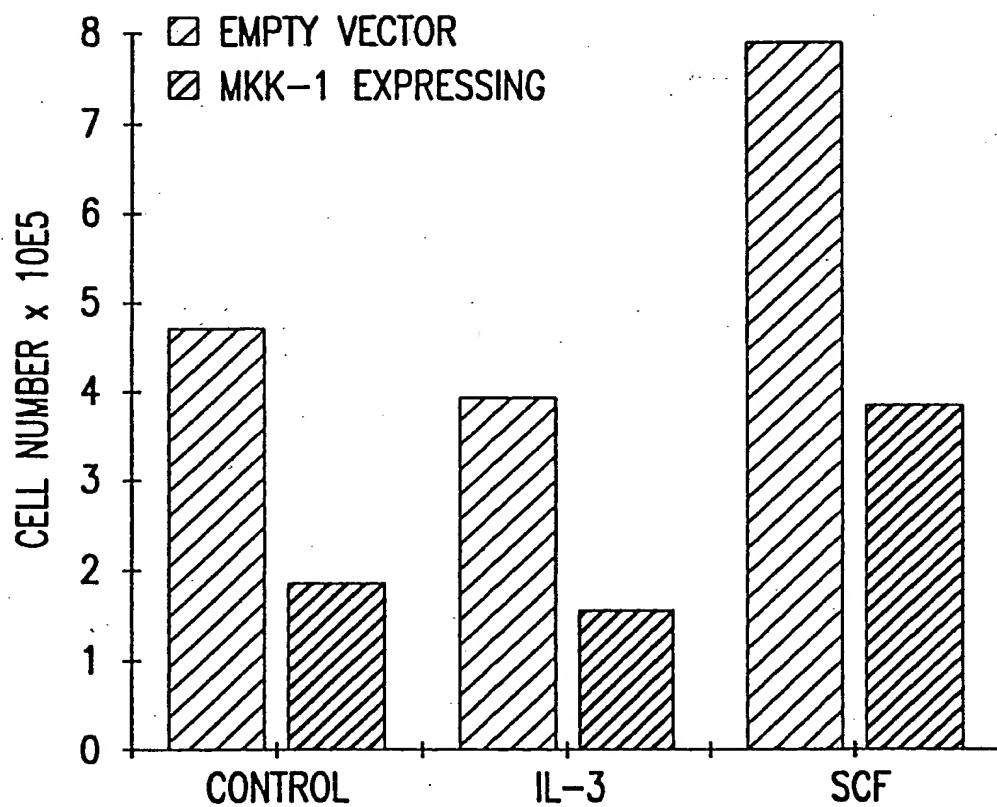
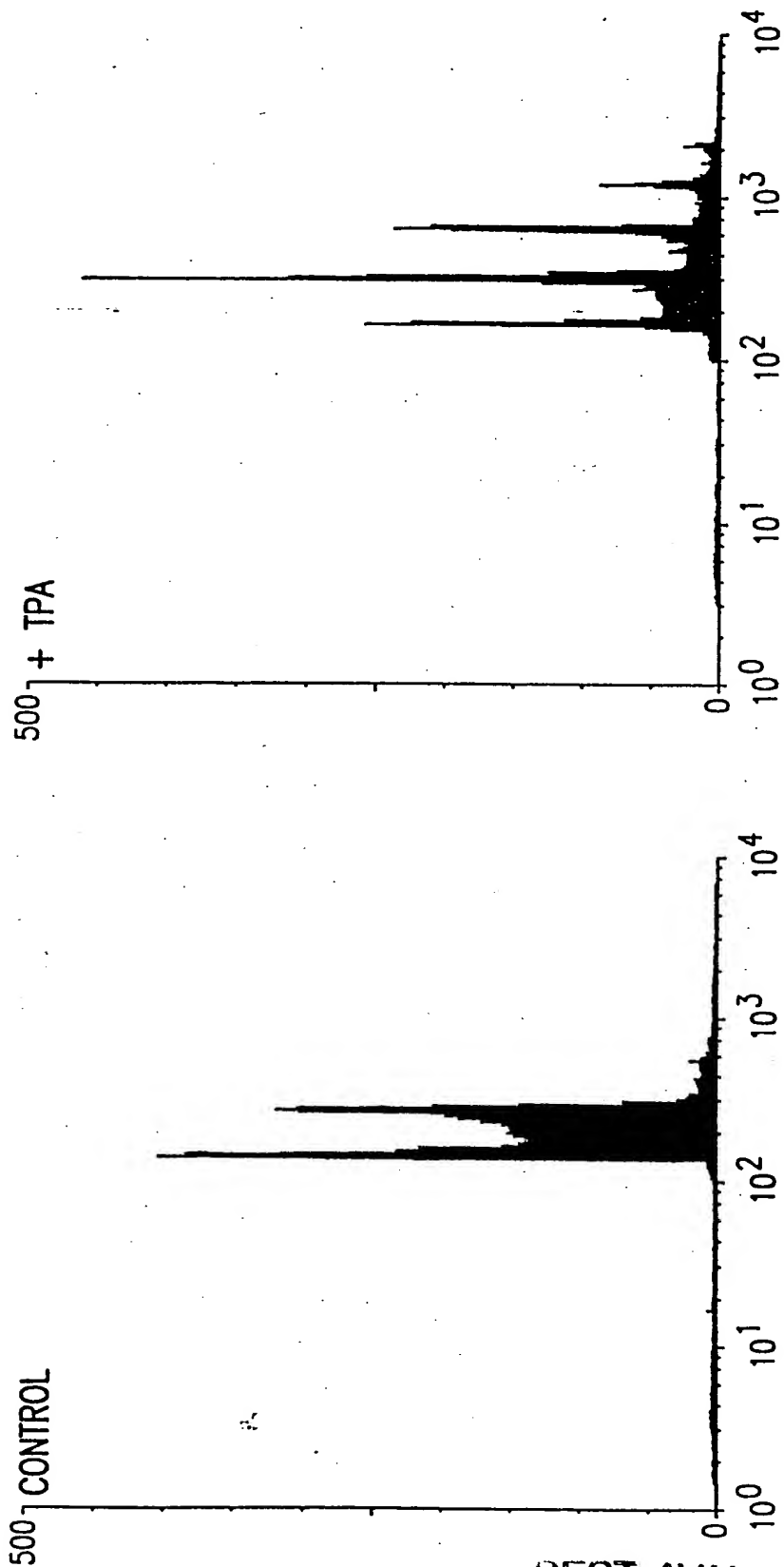


FIG.13





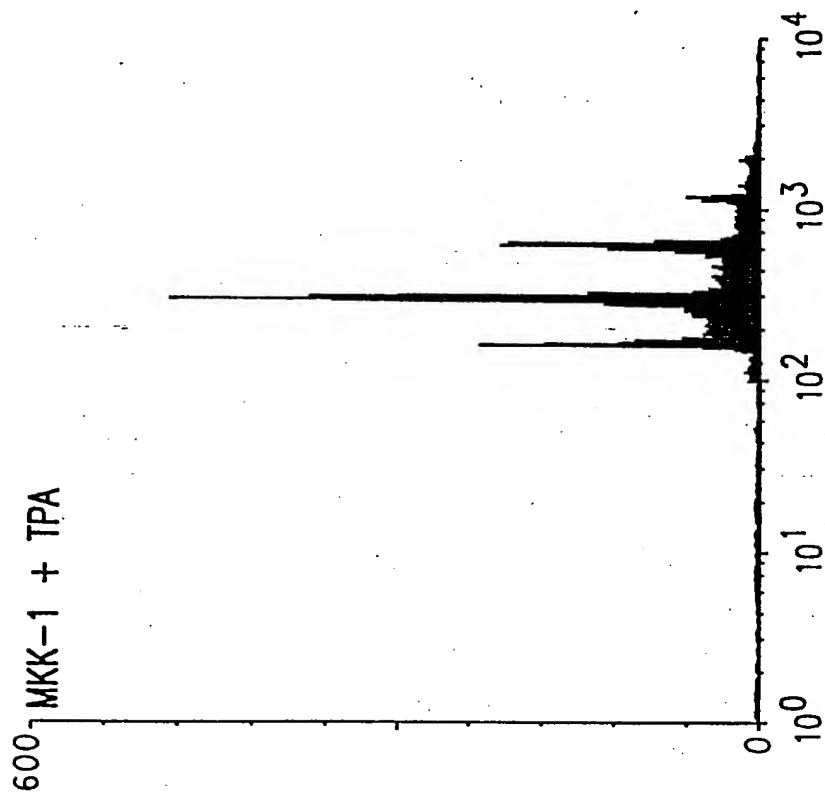


FIG.14D

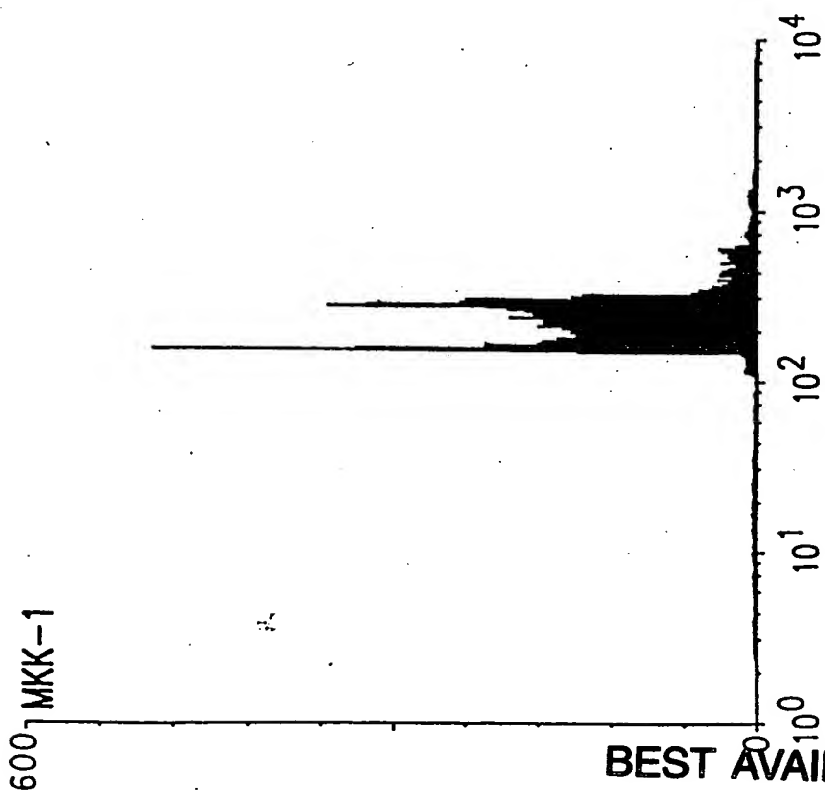


FIG.14C